1. AMENDMENTS IN THE SPECIFICATION

Please amend the Specification as follows:

In the Paragraph beginning at Page 3, line 24, spanning Page 4, line 5:

The present invention overcomes these and other limitations inherent in the prior art by providing new rAAV-based genetic constructs specifically suited for transforming mammalian cells, such as human pancreatic islet cells that encode therapeutic and prophylactic polypeptides, and in particular, serpins and/or cytokines that are useful in the treatment and/or prevention of certain types of mammalian ~~diseses~~diseases and/or dysfunctions, including, for example, diabetes and/or other dysfunctions of the pancreas.

In the Paragraph beginning at Page 5, line 10:

The invention also provides recombinant adeno-associated virus virions and pluralities of rAAV viral particles that comprise at least a first therapeutic AAV construct as disclosed herein.

In the Paragraph beginning at Page 7, line 13:

The invention also provides a method for preventing Type I diabetes in a human suspected of having, or at risk for developing Type I diabetes. The method generally involves prophylactically administering to such a patient one or more of the therapeutic ~~raAAV~~rAAV compositions disclosed herein, in an amount and for a time sufficient to prevent, delay the onset of, reduce the seriousness of, or lessen the severity of Type I diabetes in the patient.

In the Paragraph beginning at Page 8, line 13:

In other embodiments, a polynucleotide encoding one or more therapeutic cytokine polypeptides, such as BDNF, CNTF, CSF, EGF, FGF, G-SCF, GM-CSF, gonadotropin, IFN-α, IFN-β, IFN-γg, IGF-I, IGF-II, M-CSF, NGF, PDGF, PEDF, TGF, TGF-β2, TNF, VEGF, prolactin, somatotropin, or XIAP1 is placed under the control of ~~the suitabler~~a suitable promoter and used to produce therapeutically-effective levels of the biologically-active encoded therapeutic polypeptide when suitable mammalian cells comprise the rAAV genetic construct.

In the Paragraph beginning at Page 9, line 1:

In other embodiments, a polynucleotide encoding one or more therapeutic serpin polypeptides, such as any one of those described in Section 5.5 hereinbelow, and as included in SEQ ID NOs:1-SEQ ID NO:50 is placed under the control of ~~the suitabler~~a suitable promoter, and used to produce therapeutically-effective levels of the biologically-active encoded therapeutic polypeptide in suitable mammalian cell that comprise the rAAV genetic construct.

At Page 11, lines 9-14:

Likewise, the present invention provides rAAV vectors that encode one or more therapeutic ~~polypeptid~~polypeptide(s) that comprise(s), consist(s) essentially of, or consist(s) of, at least a first sequence region that preferably shares at least about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, or about 90%, or higher sequence identity with the amino acid sequence of any one of SEQ ID NO:1 to SEQ ID NO:50.

In the Paragraph beginning at Page 16, line 10:

Polynucleotides that encode a therapeutic polypeptide may generally be used for production of the polypeptide, *in vitro* or *in vivo*. Polynucleotides that are complementary to a coding sequence (*i.e.*, antisense polynucleotides) may also be used as a probe or to inhibit the biological activity of a particular selected ~~sequence~~ sequence. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA.

In the Paragraph beginning at Page 16, line 16:

Any of the disclosed polynucleotides may be further modified to increase stability *in vivo*. ~~The is~~This is particularly relevant when the therapeutic construct delivered by the disclosed AAV vectors is an antisense molecular or a ribozyme.

At Page 18, line 7:

Exemplary pharmaceutical ~~compostions~~compositions and methods for their administration are discussed in significant detail hereinbelow.

At Page 20, line 12:

FIG. 7A and **FIG. 7B** ~~shows~~show rAAV cytokine gene delivery and the natural history of insulin autoantibodies (IAA) in NOD mice.

At Page 25, lines 11-14:

Some serpins, such as ovine uterine serpin, inhibit a wide variety of immune responses, including mixed ~~lyphocyte~~lymphocyte reaction, mitogen-stimulated lymphocyte proliferation, T cell-dependent antibody production and immunological rejection of the fetal allograft (Peltier and Hansen, 2001).

At Page 29, lines 14-15:

Sequence analysis supports a recombination event between ~~seroType 1 and 2~~serotype 1 and serotype 2.

At Page 30, lines 17-19:

As used herein, a recombinant or heterologous promoter is intended to refer to a promoter that is not normally associated with [[an]]a cytokine- or a serpin-encoding gene in its natural environment.

In the Paragraph beginning at Page 37, line 7:

It will also be understood that, if desired, nucleic acid segments, RNA, DNA or PNA compositions that express one or more of the therapeutic gene products as disclosed herein may be administered in combination with other agents as well, such as, *e.g.*, proteins or polypeptides or various pharmaceutically-active agents, including one or more systemic or ~~localized administrations~~localized administration(s) of serpin or cytokine polypeptides, biologically active fragments, or variants thereof.

In the Paragraph beginning at Page 38, line 8:

In certain circumstances it will be desirable to deliver the AAV vector-based therapeutic ~~constracts~~constructs in suitably formulated pharmaceutical compositions disclosed herein either subcutaneously, intraocularly, intravitreally, parenterally, intravenously, intramuscularly, intrathecally, or even orally, intraperitoneally, or by nasal inhalation, including those modalities as described in U. S. Patent 5,543,158; U. S. Patent 5,641,515 and U. S. Patent 5,399,363 (each specifically incorporated herein by reference in its entirety).

At Page 47, lines 12-13:

~~Varioius~~Various methods are well-known to artisans in the field, including for example, those techniques described herein:

At Page 72, lines 18-19:

5.1.8 AAV SEROTYPE I MEDIATED 1000-FOLD HIGHER ~~TRANSCDUCTION~~TRANSDUCTION EFFICIENCY IN SKELETAL MUSCLE

At Page 74, lines 5-6:

Four separate transplant combinations will be used. In the first set of experiments, islet from C57bl/6 donor will be transplanted to diabetic nude (T cell ~~immunodeficent~~immunodeficient) mice.

At Page 75, lines 4-7:

This donor-recipient combination allows ~~to~~ pinpointing the role of recurrent autoimmunity, in the absence of confounding allorecognition phenomena, on islet graft loss, and the efficacy of gene delivery in preventing it.

At Page 98, line 10:

5.3.3 ~~IMMUNOREGULATON~~IMMUNOREGULATION OF CELLULAR IMMUNE RESPONSES

At Page 101, lines 2-4:

rAAV vectors are capable of stable *in vivo* expression (Flotte *et al.*, 1993; Kaplitt *et al.*, 1994; Xiao *et al.*, 1996; Kessler *et al.*, 1996; Fisher ~~*etal.*~~*et al.*, 1997; Clark *et al.*, 1997) with low immunogenicity (Jooss *et al.*, 1998).

In Table 3 At Page 103:

TABLE 3

	Donor to Recip	**Donor to Recip**	**Donor to Recip**	**Donor to Recip**
I. Function transplant type	C57BL/6 into Nude (strep) Allogeneic			
	Group A	Group B	Group C	Group D
II. Protection Transplant type	C57BL/6 into NOD (~~femal~~female)	NOD (male) into (NOD) female	C57BL/6 into NOD (male/strep)	C57Bl/6 into BalbC (strep)
	Allo/Autoimm.	Syng/Autoimm.	Allogeneic	Allogeneic

At Page 104, line 16:

5.3.10 ~~IMMUNOSUPPRESION~~IMMUNOSUPPRESSION